Special Focus, Ocular Surface and Cornea, Original Article

# Demographics and clinical profile of patients with ocular *Calotropis* poisoning in India

*Varsha M Rathi[1]*, Anthony Vipin Das[2,3]*, Mayank Mahajan[4], Rohit C Khanna[1,3,5,6]*

**Purpose:** To describe the clinical profile of patients with ocular *Calotropis* poisoning presenting to a multitier ophthalmology hospital network in India. **Methods:** This cross-sectional hospital-based study included 2,047,360 new patients presenting between August 2010 and March 2020. Patients with a clinical diagnosis of *Calotropis* poisoning in at least one eye were included. The data were collected using an electronic medical record system. Descriptive statistics using mean ± standard deviation and median with inter-quartile range (IQR) were used to elucidate the demographic data. Chi-square test was done for univariate analysis. **Results:** Overall, 362 (0.018%) new patients were diagnosed with ocular *Calotropis* poisoning during the study period. The mean age of the patients was 44.10 ± 18.61 years. The incidence rates were 0.013% in children and 0.018% in adults. Males were 57.46% and 87.29% had unilateral affliction. A significant number of patients presented from the rural geography (59.67%) and were from the higher socioeconomic class (72.65%). About a fourth of the patients were homemakers (23.48%) followed by agriculture workers (18.23%). Of the 408 affected eyes, 49.26% had mild visual impairment (<20/70) followed by moderate visual impairment (>20/70 to ≤ 20/200) in 23.28%. The most common clinical signs were conjunctival congestion (61.03%), descemet membrane folds (57.35%), stromal edema (30.39%), and corneal epithelial defect (24.51%). **Conclusion:** *Calotropis* poisoning in individuals seeking eye care in India is very rare. It is commonly unilateral and occurs more in the rural geography. It is common in middle-aged males and may affect vision due to involvement of the cornea.

**Access this article online**

**Website:** www.ijo.in

**DOI:** 10.4103/ijo.IJO_3434_20

**Quick Response Code:**

**Key words:** *Calotropis*, electronic medical records, India

*Calotropis* is a milkweed and belongs to family *Asclepiadeae*. The two common species are procera and gigantea. These perennial plants produce white or pink flowers and are found in most parts of the world with a warm climate in dry, sandy, and alkaline soils as in the tropics of Asia, Africa, South America, Saudi Arabia, Thailand, Sri Lanka, India, and China.[1,2] In India, it is more common in the states of Punjab, Bihar, Maharashtra, Rajasthan, Gujarat, and in South India.[3,4] These plants are used for their medicinal activity and the effect is either therapeutic or toxic depending on the mode of use and dose.[1,5] Flowers, garlands, and leaves of *Calotropis* plant are of Vedic significance and are used for worshipping Gods in India.[2] The plant exudes copious milky sap or latex.[2,4,6] Accidental contact during plucking of flower or inoculation of latex may cause inflammation of the eye resulting in toxic keratitis, endothelial cell damage, corneal edema and iridocyclitis.[2-4,6,7]

The aim of this study was to describe the clinical profile of patients with ocular *Calotropis* poisoning presenting to a multitier ophthalmology hospital network in India.

## Methods

This cross-sectional observational hospital-based study included all new patients presenting between August 16, 2010 and March 30, 2020 to an ophthalmology network located in 200 different geographical locations spread across four states (Telangana, Andhra Pradesh, Odisha, and Karnataka) of India.[8] The patient or the parents or guardians of the patient filled out a standard consent form for electronic data privacy at the time of registration. None of the identifiable parameters of the patient information were used for analysis of the data. The study adhered to the Declaration of Helsinki and was approved by the Institutional Ethics Committee. The clinical data of

[1]Allen Foster Community Eye Health Research Centre, Gullapalli Pratibha Rao International Centre for Advancement of Rural Eye Care (GPRICARE), L V Prasad Eye Institute (LVPEI), Hyderabad, [2]Department of EyeSmart EMR & AEye, LVPEI, Hyderabad, Telangana, [3]Indian Health Outcomes, Public Health and Economics Research Center, LVPEI, Hyderabad, Telangana, [4]GPRICARE, LVPEI, Hyderabad, Telangana, [5]Brien Holden Eye Research Centre, LVPEI, Banjara Hills, Hyderabad, [6]School of Optometry and Vision Science, University of New South Wales, Sydney, Australia

*Equal Contribution to the Paper

Correspondence to: Dr. Varsha M Rathi, Allen Foster Community Eye Health Research Centre, Gullapalli Pratibha Rao International Centre for Advancement of Rural Eye Care (GPRICARE), L V Prasad Eye Institute, L V Prasad Marg, Banjara Hills, Hyderabad - 500 034, Telangana, India. E-mail: varsharathi@lvpei.org

Received: 20-Nov-2020 Revision: 25-Feb-2021
Accepted: 08-Mar-2021 Published: 25-Aug-2021



**Cite this article as:** Rathi VM, Das AV, Mahajan M, Khanna RC. Demographics and clinical profile of patients with ocular *Calotropis* poisoning in India. Indian J Ophthalmol 2021;69:2417-20.

each patient who underwent a comprehensive ophthalmic examination were entered into a browser-based electronic medical records system (eyeSmart EMR) by uniformly trained ophthalmic personnel and supervised by an ophthalmologist using a standardized template.[9] Approval was obtained from the Institutional Ethics Committee and adhered to the tenets of the Declaration of Helsinki.

A total of 2,047,360 new patients of all ages presented to the network during the study period. The eyeSmart EMR was initially screened for patients with (i) complaints of falling of *Calotropis* plant juice/milky fluid in the eye, (ii) local colloquial reference to the plant as *Jilledu* in the chief complaints, (iii) final ocular diagnosis of toxic keratitis/chemical injury cornea in one or both eyes, or (iv) keyword search for *Jilledu* in plan of treatment column. A total of 362 patient records were identified using this search strategy and were included as cases in the study.

The data of 362 new patients included in this study were retrieved from the electronic medical record database and segregated into a single excel sheet. The columns included the data on demographics, clinical presentation, and ocular diagnosis and were exported for analysis. The excel sheet with the required data was then used for analysis using the appropriate statistical software. Standardized definitions were used for occupation and socioeconomic status. The geographic categorization of the districts of India was performed in accordance to the National Sample Survey Organization (NSSO) which defines "rural" as an area with a population density of up to 400 per square kilometer.[10] The Constitution (seventy-fourth Amendment) Act, 1992 defines a metropolitan area in India as, an area having a population of one million or more, comprised in one or more districts and consisting of two or more municipalities or panchayats or other contiguous areas, specified by the Governor by public notification to be a metropolitan area. The remaining districts were classified as urban.[11] The visual acuity was classified according to the WHO guidelines.[12]

### Statistical analysis

Descriptive statistics using mean ± standard deviation and median with inter-quartile range (IQR) were used to elucidate the demographic data. Chi-square test (Stata software, Stata Corp. 2015. College Station, TX: Stata Corp LP) was used for univariate analysis to detect significant differences in the distribution of demographics features between patients with *Calotropis* poisoning and the overall population.

## Results

Of the 2,047,360 new patients who presented across the network during the study period, 362 patients were diagnosed with *Calotropis* poisoning in at least one eye, translating into an incidence rate of 0.018% (95%CI: ± 0.0002%) or 177/million population.

The mean age of the patients with exposure to *Calotropis* plant juice was 44.10 ± 18.61 years, whereas the median age was 47 (IQR: 32–59) years. The incidence of *Calotropis* poisoning in each age-decade is presented in Fig. 1. The overall incidence was 0.013% (37/287,434) in children and 0.018% (325/1,759,926) in adults. The incidence of *Calotropis* poisoning increased steadily from the third decade of life peaking in the sixth decade, followed by a gradual decline in the subsequent decades.

There were 208 (57.46%) male and 154 (42.54%) female patients. The overall incidence of *Calotropis* poisoning was greater ($P = 0.02$) in males (0.019%; 208/1,086,489) as compared to females (0.016%; 154/960,871). Among the patients, the mean and median age were 45.70 ± 18.79 and 49.5 (IQR: 33 to 60) years for males and 41.94 ± 18.14 and 45 (IQR: 28 to 55) years for females, respectively. The overall mode was 60 years; 60 years for male and 49 years for females.

There were 216 (59.67%) patients with *Calotropis* poisoning from rural districts, 135 (37.29%) from urban districts and 11 (3.04%) from metropolitan regions. The overall incidence was significantly higher ($P = 0.000373$) in rural communities (0.023%; 216/926,534) as compared to the urban community (0.015%; 135/925,508).

There were 99 (27.35%) patients with *Calotropis* poisoning from the lower socio-economic class, 258 (71.27%) from the lower middle class and 5 (1.38%) from the upper middle class. The overall incidence was significantly higher ($P < 0.0001$) in the higher socio-economic strata (0.018%; 263/1,502,118) as compared to lower socioeconomic strata (0.018%; 99/545,242).

Of the 362 patients with *Calotropis* poisoning, 85 (23.48%) were homemakers; 66 (18.23%) were agricultural workers, 61 (16.85%) were professionals, 51 (14.09%) were manual laborers, 44 (12.15%) were students, 22 (6.08%) were currently not employed (retired or unemployed); and in the remaining 33 (9.12%) the occupational category was not available.

The ocular *Calotropis* poisoning was unilateral in 316 (87.29%) patients and bilateral in 46 (12.71%) patients. In the 408 affected eyes, 201 eyes (49.26%) had mild or no visual impairment (>20/70), 95 eyes (23.28%) had moderate visual impairment (<20/70 to 20/200), 13 eyes (3.19%) had severe visual impairment (<20/200 to 20/400), 63 eyes (15.44%) had blindness 3 (<20/400 to 20/1200), 6 eyes (1.47%) had blindness 4 (<20/1200 to PL), 3 eyes (0.74%) had blindness 5 (NPL) and in 27 eyes (6.62%) the visual acuity was undetermined or unspecified.

In the 408 affected eyes, there was conjunctival congestion in 249 (61.03%) eyes, papillae in 16 (3.92%) eyes and a very small subset had chemosis in 5 (1.23%) eyes and discharge in 4 (0.98%) eyes. In the cornea, there was descemet membrane folds in 234 (57.35%) eyes, stromal edema in 124 (30.39%) eyes, epithelial defect in 100 (24.51%) eyes, superficial punctate keratitis in 102 (25%) eyes, corneal scar in 22 (5.39%) eyes and infiltrate in 15 (3.68%) eyes. Fig. 2 shows the slit-lamp biomicroscopy findings after *Calotropis* poisoning.

The ocular *Calotropis* poisoning was managed significantly through medical treatment. Steroid eye drops were prescribed in 211 (58.29%) patients, lubricants were prescribed in 174 (48.07%) patients, antibiotic eye drops in 127 (35.08%) patients and mydriatics in 103 (28.45%) patients. Surgical treatment was rarely required and amniotic membrane graft was performed in 3 (0.83%) patients. The mean number of visits of the patients was 1.96 ± 5.28.

There is a distinct month-wise variation associated with ocular *Calotropis* poisoning with the highest incidence seen in the month of March (54/164,630; 0.33%), February (57/182,329; 0.031%) followed by January (47/174028; 0.027%) and this was statistically significant. The least number of

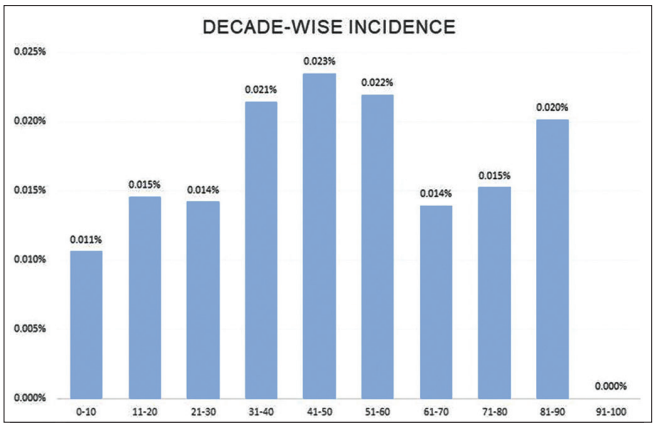


**Figure 1:** Incidence of ocular *Calotropis* poisoning in each decade of age. The incidence of *Calotropis* poisoning increased steadily from the third decade of life peaking in the sixth decade, followed by a gradual decline in the subsequent decades

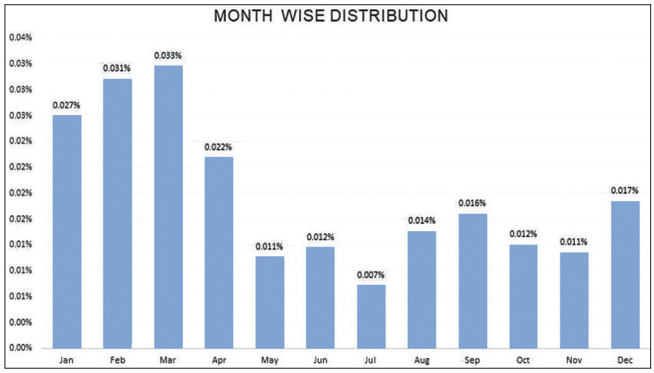


**Figure 3:** Month-wise distribution of ocular *Calotropis* poisoning. The incidence of *Calotropis* poisoning was the highest in the month of March (0.033%) and the lowest in July (0.007%)

cases were seen in July (13/177,379;0.007%). The month-wise distribution is described in detail in Fig. 3.

## Discussion

The present study reports the clinical and demographic features in a large cohort of patients exposed to juice of *Calotropis* from the indigenously developed electronic database of a multitier ophthalmology hospital network located in Southern India with its secondary centers located in rural areas. *Calotropis* is used for its medicinal value as medicinal as well as for worship. The latex of *Calotropis procera* contains several alkaloids (such as Calotropin, Catotoxin, Calcilin, Gigantin). Waikar and Srivastava have shown that the sap of *Calotropis* is acidic.[3] Shivkumar and Kumar have shown that *Calotropis* contains histamine and also causes release of histamine from mast cells which results in the inflammatory action.[13] They also have shown role of prostaglandin in the inflammation.[14] The inflammation is rapid onset and short lasting.[13]

A significant number of patients in rural areas had the poisoning compared to urban and metropolitan areas. This may either be due to the use as medicinal plant or while using as a flower for worshipping. Shenoy *et al*. have reported a case of *Calotropis* poisoning when it was used for the management of chalazion.[15]

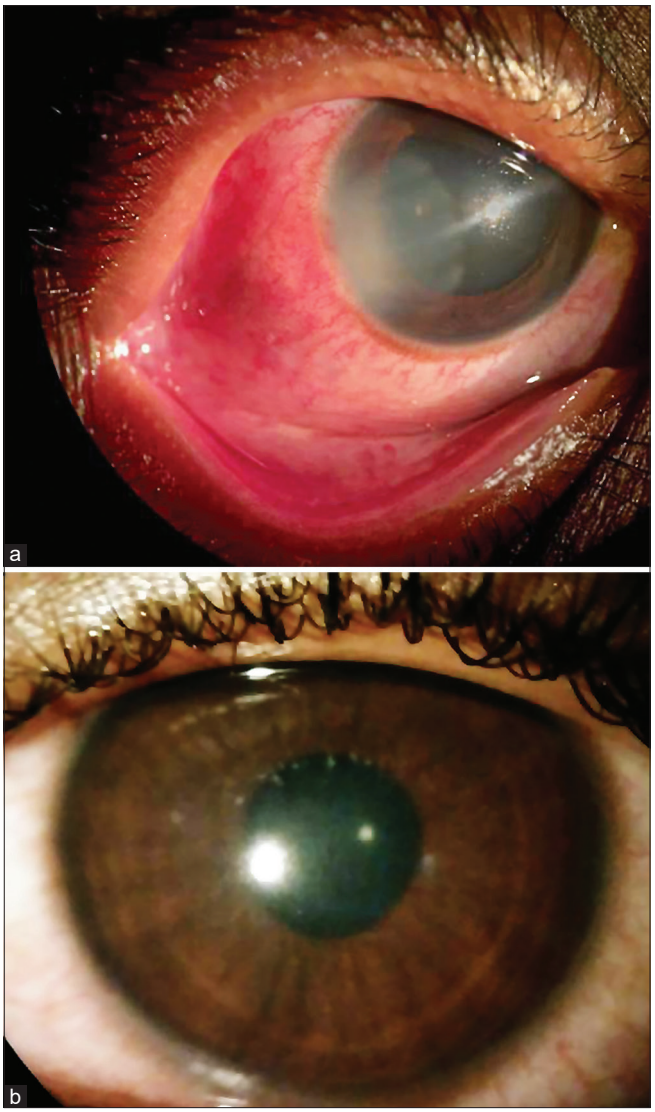


**Figure 2:** (a) Diffuse slit-lamp photograph showing conjunctival congestion and dense stromal edema with descemet membrane folds, no KPs—after exposure to *Calotropis*. Patient received topical corticosteroids and cornea cleared. (b) Diffuse slit-lamp photo showing quiet conjunctiva and subtle stromal edema and DM folds. One may confuse this with disciform keratitis and a proper history will clinch the diagnosis of *Calotropis* keratitis. This patient too responded to topical corticosteroids

The overall incidence was significantly higher in the higher socioeconomic stata. Being a retrospective study, the activity that caused the poisoning is not available. However, occupation wise, homemakers had it more compared to others.

The mean age of the patients was 44.10 ± 18.61 years in this study compared to Basak *et al*. (mean: 41.3 ± 9.3).[2] The incidence was higher in males (57.46%) as compared to females. Though male preponderance is there, it is low but similar to Basak *et al*., who had male preponderance in 83% ($n$ = 29 cases).[2] As against this, Pandey *et al*. have reported 90% of cases were females in their series of 10 cases.[4] The incidence increased from third to 6$^{th}$ decade and then reduced indicating the young active people. The difference in the gender distribution as compared

to other studies is possible because of the larger sample size in our cohort.

The poisoning was more unilateral (87.29%) compared to bilateral. This is similar to Basak *et al*. who had 86% of their patients had right eye involvement. Accidental rubbing of right eye when one handles flowers or touches eye unknowingly can cause the poisoning.[2]

In this cohort, conjunctival congestion was more common and noted in 61.03% eyes with less than 5% patients having papillae and a very small subset had chemosis in 5 (1.23%) eyes. Basak *et al*. have reported 100% of patients having conjunctival congestion.[2] In the cornea, there were descemet membrane folds in 234 (57.35%) eyes and stromal edema in 124 (30.39%) eyes, as against 100% of patients from Basak *et al*. study.[2] The presence of epithelial irregularities such as presence of epithelial defect and superficial punctate keratitis was noted in 202 eyes (49.51%) eyes compared to the presence of epithelial defect in 3 (10.3%) eyes as reported by Basak *et al*.[2] Corneal scar was noted in 22 (5.39%) eyes and presence of active infiltrate in 15 (3.68%) eyes. The presence of active infiltrate may be due to secondary infection in presence of epithelial defect.

The limitations of the study include missing of the cases due to nondocumentation of the history of the mode of injury due to *Calotropis* or *Jilledu* (colloquial word) in the electronic medical record.

The highest incidence was in the month of March (54/164,630; 0.33%) and February (57/182,329; 0.031%). This is similar to Basak *et al*. where they have reported that that the poisoning is more common in the months of February to April.[2] This may be due to the special occasion of worship of a particular God in the month for whom the flowers are used.

## Conclusion

Awareness about *Calotropis* causing corneal edema and DM folds and differentiating it from viral stromal keratitis is important. Public education is needed to avoid the accidental exposure to this widely distributed tree in India and many tropical countries.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Financial support and sponsorship

Hyderabad Eye Research Foundation.

### Conflicts of interest

There are no conflicts of interest.

## References

1. Yaniv Z, Koltai H. Calotropis procera, Apple of Sodom: Ethnobotanical review and medicinal activities. Isr J Plant Sci 2018;65:55-61.
2. Basak SK, Bhaumik A, Mohanta A, Singhal P. Ocular toxicity by latex of Calotropis procera (Sodom apple). Indian J Ophthalmol 2009;57:232-4.
3. Waikar S, Srivastava VK. Calotropis induced ocular toxicity. Med J Armed Forces India 2015;71:92-4.
4. Pandey N, Chandrakar AK, Garg ML, Patel SS. Calotropis procera -induced keratitis. Indian J Ophthalmol 2009;57:58-60.
5. Lima RC, Silva MC, Aguiar CC, Chaves EM, Dias KC, Macedo DS, *et al.* Anticonvulsant action of Calotropis procera latex proteins. Epilepsy Behav 2012;23:123-6.
6. Al-Mezaine HS, Al-Rajhi AA, Al-Assiri A, Wagoner MD. Calotropis procera (ushaar) keratitis. Am J Ophthalmol 2005;139:199-202.
7. Tomar VP, Agarwal PK, Agarwal BL. Toxic iridocyclitis caused by calotropis. J All India Ophthalmol Soc 1970;18:15-6.
8. Rao GN, Khanna RC, Athota SM, Rajshekar V, Rani PK. Integrated model of primary and secondary eye care for underserved rural areas: The L V Prasad Eye Institute experience. Indian J Ophthalmol 2012;60:396-400.
9. Das AV, Kammari P, Vadapalli R, Basu S. Big data and the eyeSmart electronic medical record system-An 8-year experience from a three-tier eye care network in India. Indian J Ophthalmol 2020;68:427-32.
10. Available from: http://mospi.nic.in/sites/default/files/Statistical_year_book_india_chapters/local_bodies.pdf?download=1. [Last acessed on 2019 May 04].
11. Available from: https://mhrd.gov.in/sites/upload_files/mhrd/files/upload_document/74amend.pdf. [Last accessed on 2019 May 04].
12. World Health Organization. Change the Definition of Blindness [PDF file]. 2008. Available from: https://www.who.int/blindness/Change%20the%20Definition%20of%20Blindness.pdf13.13.
13. Shivkar YM, Kumar VL. Histamine mediates the pro-inflammatory effect of latex of Calotropis procera in rats. Mediators Inflamm 2003;12:299-302.
14. Kumar VL, Shivkar YM. Involvement of prostaglandins in inflammation induced by latex of Calotropis procera. Mediators Inflamm 2004;13:151-5.
15. Shenoy R, Bialasiewicz A, Khandekar R, Al Barwani B, Al Belushi H. Traditional medicine in Oman: Its role in ophthalmology. Middle East Afr J Ophthalmol 2009;16:92-6.